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Teicoplanin use and emergence of *Staphylococcus haemolyticus*: is there a link?

We read with great interest the meta-analysis of Vardakas *et al.* [1] which evaluated the effectiveness and safety of perioperative prophylaxis with teicoplanin, compared with first- or second-generation cephalosporins, in patients undergoing orthopaedic and vascular surgery. The authors concluded that both regimens are equally effective in terms of the development of infections, adverse effects and mortality, but suggested that large-scale use of teicoplanin cannot be recommended because of the likely emergence of resistance. This phenomenon seems to be particularly important with *Staphylococcus haemolyticus*, an emerging cause of nosocomial infection, which is now the third most common organism among clinical isolates of methicillin-resistant staphylococci [2].

In our hospital, teicoplanin is not used for perioperative anti-infective prophylaxis, but is much used for therapy. Indeed, since the early 1990s, 16 000–18 000 200-mg vials have been administered annually to our patients, compared with only 6000–8000 500-mg vials of vancomycin [3]. Under these circumstances, *S. haemolyticus*, usually exhibiting methicillin resistance, has been isolated increasingly from hospitalised patients, particularly those at highest risk of infection. During the period 2000–2003, one of the hospital microbiology laboratories, which received mainly clinical specimens from post-trauma/post-surgery and post-transplantation intensive care units, found that *S. haemolyticus* was the second most common cause of coagulase-negative staphylococcal (CNS) bacteraemia (after *Staphylococcus epidermidis*), accounting for 22–24% of CNS isolates annually. The annual rate of teicoplanin resistance among these *S. haemolyticus* blood isolates was 11–29%. Studying patients with haematological malignancies during the period June 2000–January 2001 [4], we identified 22 (8.7%) methicillin-resistant *S. haemolyticus* (MRSH) among 252 bacterial and fungal blood isolates. MRSH was again the second most common CNS isolate from blood cultures, accounting for 17.8% of 123 CNS isolates (methicillin-susceptible CNS were not identified to the species level).

It should be stressed that *S. haemolyticus* resistance rates to glycopeptides may be underestimated, because most isolates, which are apparently susceptible to these drugs according to the usual susceptibility tests, may display growth of isolated colonies at very high vancomycin or teicoplanin concentrations [5]. Thus ten of 20 *S. haemolyticus* bacteraemia isolates from patients in various high-risk areas of our hospital were fully-resistant to teicoplanin. Most of these teicoplanin-resistant isolates were related genetically and clonally distributed. Moreover, seven of the remaining ten isolates, which were apparently susceptible, were shown to be heteroresistant to teicoplanin following further analysis.

The clinical significance of *S. haemolyticus* is not yet defined fully. Our data show that isolation of MRSH from bacteraemic patients with haematological malignancies is associated with negligible morbidity/mortality rates; however, MRSH isolates with decreased susceptibility (MIC 16 mg/L) or resistance (MIC ≥32 mg/L) to teicoplanin show a lower clinical response rate to this glycopeptide than do isolates that are fully susceptible [4]. More importantly, preliminary data from an ongoing retrospective clinical and microbiological analysis, currently including 15 well-documented MRSH infections, show that MRSH may be a cause of severe disease, including infective endocarditis (infections of three prosthetic valves and one native valve infection), post-neurosurgery meningitis (five cases, of which four were shunt-associated infections), prosthetic joint infection (two cases), and other foreign body-associated infections (four cases). Most of these infections were caused by isolates that were resistant to teicoplanin, and poor susceptibility *in vitro* was associated with clinical failure of teicoplanin therapy.

In conclusion, it seems that prophylaxis with teicoplanin may be considered in hospital settings where the development of infections with multi-resistant staphylococci is likely, provided that rigorous surveillance and monitoring of the possible nosocomial spread of teicoplanin-resistant *S. haemolyticus* is also performed.

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Turkish isolates of *Helicobacter pylori* belong to the Middle Eastern genotypes

We were interested to read the recent accounts in *CMI* regarding the distribution of *Helicobacter pylori* genotypes in Mexico and Argentina [1,2]. Epidemiological studies suggest that the prevalence of *H. pylori* infection varies between developed and developing countries, as well as according to ethnicity, place of birth and socioeconomic factors, even among people living in the same country. Molecular epidemiological studies are important in order to elucidate the circulating genotypes.

In order to investigate the reason(s) for the high prevalence of *H. pylori* infection and gastric cancer in Turkey, the *cagA, vacA* and *iceA* genes were used as molecular markers to characterise isolates from patients infected with *H. pylori*. In total, 87 isolates of *H. pylori* from adult patients were investigated. Antral gastric biopsy samples taken from patients were cultured using standard methods [3]. The presence of the *cagA* gene, the mid-region of the *vacA* gene, the signal sequences of the *vacA* gene, and the *iceA* genotype were determined by PCR as described previously [4–6]. For *vacA*, the most common genotype was *vacA m2s2*, followed by *vacA m2s1a*. In total, 40 (46%) isolates were *cagA*-positive, and 62 (71.3%) isolates were *iceA* positive. Of these, 28 were positive for *iceA1* only, 12 for *iceA2* only, and 22 for both *iceA1* and *iceA2*.

The fact that 37% and 33% of the isolates, respectively, belonged to the *s1* and *s2* genotypes, and that 46% of the isolates were *cagA*-positive, suggests a strong similarity to the Middle Eastern genotypes [7]. Moreover, the *iceA1* subtype was twice as common as the *iceA2* subtype in the present study, and a significant number of isolates possessed both *iceA1* and *iceA2*, which also indicates that Turkish isolates of *H. pylori* are similar to the Middle Eastern types.

Only a few samples were found which contained multiple genotypes, which implies that most infections in Turkey are caused by single genotypes of *H. pylori*. Twelve isolates were *vacA s1 cagA*$^+$ *iceA1* (11 patients with functional dyspepsia and one with duodenal ulcer), which are considered to be the most pathogenic strains. Only five isolates were *vacAs2m2 iceA* (*cagA*-negative), which are considered to be the least pathogenic strains [8].

The present study failed to determine the genotypes of several isolates, indicating that mutation had occurred at the primer-binding sites of the genes investigated. *H. pylori* is one of the most genetically diverse bacterial species, and this mutational diversity has been enhanced by extensive inter-strain gene transfer and recombination [9]. Therefore, it is probable that evolution has selected the *H. pylori* strains that are best able to colonise the population of Turkey. Future studies should focus on determining the genetic sequences of these strains.